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PSYCHOACOUSTICAL AND ELECTROPHYSIOLOGICAL ASPECTS OF CENTRAL AUDITORY DISORDER

Summary of the Doctoral Thesis
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4. DISCUSSION

Abbreviations

AAA — *American Academy of Audiology*
ABR — *Auditory brainstem response*
ANSI — *American National Standard Institute*
ANOVA — *analysis of variance*
ASHA — *American Speech Hearing Association*
A1 — *Primary auditory cortex*
CAEP — *Cortical auditory evoked potentials*
CAPD — *Central auditory processing disorder*
CF — *Characteristic frequency*
COS — *Complex olivarii superioris*
DC — *dichotic digit word test (DDWT)*
DD — *dichotic word test (DWT)*
GABA — *Gamma amyno butiryc acid*
GAD — *Glutamacid decarboxylasis*
EEG — *Electroencephalography*
ERP — *Event-related response*
FMR — *Functional magnetic resonances imaging*
ISO — *International Standard Organisation*
Hz — *hertz*
HG — *Heschl's gyrus*
JPG — *young patient group*
kOhm — *kiloohms*
MMN — *Mismatch negativity*
µV — *microvolts*
N — *control group*
NC — *Nucleus cochlearis*
RUS — *Speech reception threshold*
RUS/T — *Speech reception threshold/ noise*
SD — *Standard deviation*
STG — *Superior temporal gyrus*
VPG — *elderly patient group*

1. INTRODUCTION

1.1. Scientific and practical novelty of work

Audition is one of the most important senses, which is necessary in communication. In case of audition defects, the function damage may be in central auditory system, diagnostic of which in Latvia is limited. Central auditory processing is assessed by method of psychoacoustic diagnostics – speech audiometry. It is recommended to be performed in native language, therefore it was important to establish the required language material in native language.

Cognitive function has impact on speech audiometry; besides, active participation of patient is required. In promotion work the central auditory processing is investigated also by electrophysiological method that is not used in Latvia before – for cortical auditory evoked potentials that reflect analysis of acoustic signal in auditory cortex and that do not require active participation of patient in process of investigation.

Both investigation methods are non-invasive and provide the possibility to assess central auditory processing. By implementation of new methods there is improved illness diagnostics in clinic otolaryngology, besides they are informative also in early diagnostics of neurodegenerative illnesses and development control, as well as assessment of medical therapy efficiency.

Meanwhile there are not known guidelines for medical therapy of Central auditory disorder, therefore there is assessed impact of such medical remedies to central auditory processing that are approved to have potency stimulating neuronal metabolism. Comparison of speech reception threshold changes and changes of acoustic signal transfer speed before and after internal medical therapy is a new method to approve efficiency of central auditory disorder therapy.

Complex investigation of central auditory processing by use of psychoacoustic and electrophysiological method has been executed in the promotion work.

1.1.1. Central auditory processing and diagnostics methods

Central auditory processing includes complex sound analysis in several aspects: distinguishing of sound properties, localisation and lateralization of sound source, sound reception at masking noise and waning sound, sound reception in time, sound reception at competitive signals (dichotic listening), sound systematisation (ASHA, 2005). Diagnosis of central auditory disorders may be determined if there are stated changes of one or several functions characteristic to central auditory process that jams processing of acoustic information (AAA, 2010).

Complaints about burdensome speech reception in complicated conditions of listening and noise testifies about central auditory disorder (Bellis, 2003; Chermak, 2002; Moore, 2006; Cacace & McFarland, 2005). Pathogenesis of speech reception disorders is related to deficit of mechanisms that provides distinction of purposeful or necessary speech signals from simultaneous other sound and speech signals (Cameron & Dillon, 2008a; Wilson & Burks, 2005).

Disorders in central nervous system axon myelination, particularly in level of *corpus callosum* is considered to be one of central auditory disorder reasons (Musiek et al., 1985). Although there are still lot of uncertainties, it is considered that these disorders are determined by neurobiological changes in those structures of central nervous system that perceives and analyses acoustic signal (Moore, 2006). It is known that reception of audition and speech is made by two mechanisms – analysis of sound signal and linguistic processing of this information (Kalikow et al., 1977).

Speech reception is impacted by sound signal properties as well as cognitive factors (Bellis, 2003; Chermak, 2002; Moore, 2006; Cacace & McFarland, 2005). Binaural audition, listening by both ears is important in order to perceive speech in noise, distinguishing certain signal among others. Binaural audition is provided by mutual functionality of cerebrum and audition structure right and left side. In level of cortex sound represents itself with all the properties in total, making the sound unit – tone, in its term the complex acoustic signals are transformed by central nervous system in comprehensible information. If impulse transmission synchronism in central auditory structures is chanced, analysis of acoustic information in cortex is impeded.

Pathogenesis of central auditory disorders involves different parts of central nervous system. Thus also diagnostics is complicated and methodology is still developing (ASHA, 2005, Legace et al., 2010; Cameron et al., 2010). However speech audiometry still is the principal method for assessment of central auditory processing. The common response reaction of all the structures involved in audition process is presented in speech audiometry. Speech audiometry tests are suggested to be performed in the native language, as there is required collaboration with patient and his active participation as well as because it is good to reduce impact of cognitive functions (Wilson et al., 2004; Cameron et al., 2006a).

In order to reflect the real audition sense, sentences of everyday speech would be more suitable for determination of speech reception threshold (Plomp, 1978; Cameron et al., 2011). Important function of central auditory is dichotic reception – ability to analyse the selection of the heard, dividing attention between simultaneously perceived different acoustic signals in each ear. Dichotic speech reception tests are considered to be audiometry investigations of informative speech, as result is less impacted by peripheral auditory structure. (Hällgren et al., 1998; Kimura, 2011).

Electrophysiological investigations, cortical auditory evoked potentials (CAEP) are neurophysiological investigation method – type of electroencephalography, during which sound stimuli are performed to the patient in earphones, so activating neurons (Song et al., 2008). Electric cortical auditory evoked potentials are generated by synchronous activity of great number of neurons, responding to sound stimuli (Coles & Mason, 1984; Rickards et al., 1996; Moore 2006) that are registered from scalp surface electrodes.

CAEP advantage is reduced impact of several factors, i.e. measuring may be performed without listening task to the subject that need involvement of attention and cognitive function. For assessment of cortex sound analysis processes in order to adjust for usage in daily practice, cortical auditory evoked potentials are surveyed.

Response wavy curve morphology of cortical auditory evoked potentials is established by pikes that have occurred in the result of positive and negative voltage changes – pike peaks or CAEP components (Bukard et al., 2010). They are denotated according polarity on the curve: positive – P and negative – N pikes. P and N components are numbered by their appearance on CAEP response curve, increasing time after signal beginning: P1, N1, P2, N2 un P3 (Alho et al., 1999; Näätanen, 2001, 2007, 2009; Moore, 2002; Bukard et al., 2010; Billings et al., 2011). Component latency (in milliseconds) complies with the time from beginning of stimuli until response of cortex. It is impacted by stimulus properties, localization of respectively reacting brain structure, and location of electrodes on scalp. When listening actively, cortical auditory evoked potential components reflect audition stimuli reception and cognitive processing that is impacted also by memory and attention. The main variable of sound signal sensory irritation is time. Quality of auditory processing is determined by successful analysis of signal in certain speed in all the auditory system stages (Broadbent, 1957). It reflects CAEP component latencies (Näätanen et al., 2007; Moore, 2002).

In order to use auditory evoked potentials method in clinics, there are required normative data and united methodology. Cortical auditory evoked potentials are divided in two categories: exogenous and endogenous potentials. Exogenous potentials are sensory potentials that may be caused by standard sound stimuli – repeated identic stimuli series. Component of exogenous potentials P1, N1 and P2 are called the obligatory components of cortical auditory evoked potentials, because their appearance curve verifies that the signal is perceived, even if no attention is turned to these stimuli (Ponton et al., 2000; Kujala et al., 2007). Usually these components appear 100 – 300 ms after beginning of stimuli and are dependent on stimuli or physical properties of sound – intensity, frequency and density (Näätanen et al., 2007). Exogenous components are followed by a longer latency endogenous component P3 that reflects internally generated, cognitive reception of stimuli related to the event (devoting attention to certain stimuli) (Sussman et al., 1999; 2006; Sanders & Poeppel, 2007). P3 has significant parameter for reception of complex acoustic signal and cognitive function related to it (Bell et al., 2010; Billings et al., 2009; Mulert et al., 2004). CAEP responses may be registered also without subject attention to stimulus, reducing involvement of cognitive function in the auditory process. These advantages of CAEP method make the diagnostics of central auditory processing more objective in comparison with speech audiometry. It was the aim of our investigation – to establish diagnostically informative CAEP methods that can be used in daily practice.

1.1.2. Neuroplasticity in the central auditory system

Dynamical changes in neurons structure and function that is made by aspiring to compensation of function deficit is defined as neuroplasticity (Gu, 2002). Due to this property of auditory cortex neurons information about acoustic signal is stored in the audition memory and together with cognitive function provides speech reception. Development of central auditory disorders is determined by several mechanisms: incorrect synchronism of nervous impulse transmission, hemisphere asymmetry in complex acoustic signal representation in nervous structures, inefficient transmission of acoustic information between hemispheres (Zatorre, 2002). In order to promote neuroplasticity of central audiometry structure, important meaning is to improvement of cerebrum tissue neuro-metabolism and neuroplasticity.

Activation of neurotransmission happens, when ions flow is modulating. Nootropos remedies are stimulating inflow of Na^+ ions through AMPA receptors and holynergic transfer activating in muscarine receptors (Winblad, 2005). $GABA^A$ receptors are participating in central auditory processing (Scott & Johnsrude, 2003). Racetams are derivatives of neurotransmitter γ-amino butyric acid (GABA) that have essential meaning in renewal of tissue membrane penetrability (Chebib, 2004). In neuron level pramiracetam, which is one of racetam derivatives, modulates neurotransmission to a range of transmitter systems, also holynergic and glutamatergic (Mooradian, 1988). One of the most important properties of piracetam is promotion of neuroplasticity.

Investigations show that nicergoline has wide range of activity in tissue and molecule mechanisms in vascular, thrombocyte and neuron level, participating in plasticity of synapses (Colquhoun et al., 1990), metabolisms and neuroplasticity (Mitra et al., 2001). Therefore nicergoline is used in therapy of different pathologies: treatment of dementias, Alzheimer disease, vascular dementias (Grutzendler & Morris, 2001), cerebrovascular diseases, peripheral vascular organic and functional member arteriopathy (Winblad et al., 2008).

Till now there was not known published surveys on pharmacotherapy regarding their impact on central auditory processing. Taking into account the results of investigation about positive efficiency of nicergoline in treatment of reception and cognitive disorders and that the pharmacological activity of nicergoline would be etiopathogenic to central auditory nervous system neurophysiology to patients with central auditory processing disorders, this remedy was used in our investigation.

When using racetamus together with blood-vessels widening remedies, cognitive function improvement is more efficient (Pugsley, 1983). According to these discoveries two preparations with different pharmacological activity in different localisations, but is similar regarding neurophysiological efficiency are used in our investigation. Until now there is not known surveys, where cortical auditory evoked potentials and speech reception threshold correlation is analysed, as well as there is not known impact of pramiracetam and nicergoline to investigations characterising central auditory.

For more than several years cortical auditory evoked potentials are used for investigation of central auditory processing, however they are not used in daily practice. There still are no data about elsewhere performed investigations in the world and comparative investigations of speech audiometry that have diagnostic value for assessment of central auditory processing.

1.2. Ethical aspects

For execution of investigation there was received agreement of Riga Stradins university Ethical committee (decision No. E-9 (2)/10.06.2010.).

1.3. Hypotheses of the work

1. Speech reception threshold and dichotic speech tests in the Latvian language – method of informative central auditory disorder diagnostic.
2. Latencies of cortical auditory evoked potentials are extended for patients with audition and speech reception disorders.
3. Speech reception parameters correlate with component latencies of cortical auditory evoked potentials.
4. Latencies of cortical auditory evoked potentials after medical therapy course reduce.

1.4. Aim of the work

Aim of work was to characterise central auditory processing, to determine psychoacoustic and electrophysiological criteria of central auditory disorder, to assess impact of medical therapy on central auditory processing in patients with central auditory disorder.

1.5. Terms of references

1. To establish sentences testes and dichotic word test for speech audiometry for adults in the Latvian language.
2. To execute speech audiometry, determining speech reception threshold and dichotic speech reception to people with normal audition and patients with auditory disorder.
3. To make measures of cortical auditory evoked potentials, to determine and analyse parameters of potentials components for people with normal audition and patients with auditory disorder.
4. To analyse correlations of cortical auditory evoked potentials parameters and correlations of speech audiometry.
5. To determine and analyse parameters of speech audiometry and cortical auditory evoked potentials to patients with central auditory disorders after medical therapy.

1.6. Amount and structure of the promotion work

Promotion work is written in the Latvian language. Promotion work has the following chapters: introduction, literature review, materials and methods, results, discussions, conclusions and references. Total work scope is 150 pages, analytically illustrative material is summarised in 18 tables and illustrated by 37 pictures, and there are three annexes. Literature references include 290 titles of used works.

2. MATERIALS AND METHODS

Promotion work is executed in Riga Stradins university Otorhinolaryngology department clinical basis – Pauls Stradins Clinical university hospital Otorhinolaryngology department during period of time from April 2007 until May 2012.

2.1. Materials

2.1.1. Characteristics of the population of the investigation

The investigation included 100 people, who were divided in two groups – control group and patients group. Control group included 30 people with normal audition and without complaints about audition disorders. The normal audition is considered to be auditory threshold in tonal audiometry that does not exceed 20 decibels (dB) in none of testable frequencies – 125, 250, 500, 1000, 2000, 4000, 6000 and 8000 hertzes (Hz).

Patient group consisted of 70 people who complained about encumbered resolution of words and difficulties to understand speech, particularly in the surrounding noise or public places, if several people are talking at the same time. Patient claims longed for one or one and a half year, in tonal audiometry auditory threshold in frequencies was from 250 until 2000 Hz, not exceeding 20 dB, but in frequencies until 8000 Hz – 3 dB.

All people included in the investigation were normally intellectually developed and none of them had psychosomatic diseases. All the participants of investigation patient group had higher education, worked mental work and their obligations were related to communication that needed normal audition. Participants of control group part were students of high school, but the others had graduated the higher educational institution. People in the control group were of age from 22 to 27 years (average age – 25.31 year, SD = 1.42), 14 were men, but 16 – women, they all had consultation at otolaryngologist with other claims, but they had no complaint on auditory disorders. The investigation participants were 70 patients that had complaints about auditory disorder; they were divided in two age subgroups. The first group of patients – 33 people in age of 31 – 40 years (average age – 35.31 year, SD = 2.54), 18 men and 15 women. The second group of patients – 37 people in age of 32 – 73 years (average age – 67.64 year, SD = 3.02), 17 men and 20 women.

Native language of all the investigation participants was Latvian so that the results of language audiometry are not impacted by language knowledge. In order to continue the compliance for involvement in the investigation, all individuals had been tested on tonal audiometry, tympanogam and made investigations of cortical auditory evoked potentials.

2.1.2. Criteria of involvement in the investigation group

Criteria of involvement for group of patients. Auditory disorders that expresses as difficulties to distinguish words and thus also difficulties to understand speech, particularly in the surrounding noise or public places, if several people are talking at the same time.

Criteria of involvement for participants of control and patient investigation group

1. No pathology in otoscopic investigation – free external auditory channel, greyish tympanic membrane with light reflex in its lower medial quadrant.
2. Normal tonal threshold of audiometry – until 15 dB in frequency of 250-4000 Hz, but up to 20 dB – in frequency of 4000-8000 Hz, making tonal audiometry with step of 5 dB.
3. Tympanometry – normal air pressure in tympanum ($P \geq 0$ dPa).
4. Morphology of cortical auditory evoked potentials curve is maintained, there are identified characteristic pike time units that complies with the age standard.
5. Patients do not have somatic of psychic diseases in anamnesis and during inspecting.
6. The right had is dominating. There is excluded the possible dominance of left hand after specific test issues according to the possible functional asymmetry of cerebral hemisphere in language reception, using Edinburgh Handedness Inventory (Oldfield, 1971), attached in Annex 1.
7. Magnetic resonance investigation of cerebrum does not state pathologic changes in auricle, tympanum, inner ear, aqueduct of inner ear and cerebrum.
8. Ultrasonography of head and neck blood vessels do not state disorders of hemodynamic.
9. Results of clinic investigations (full blood picture, biochemistry) do not exceed standard parameters.

Criteria of exclusion for all groups of investigation participants

1. Ear diseases.
2. Conductive and sensorineural hearing-impairment.
3. Extended latencies of cortical auditory evoked potentials components
4. Neurodegenerative CNS diseases.
5. Anamnesis of head traumas.
6. Chronic inner diseases.
7. Preparations of medical therapy are not used during survey.

Planning of investigation

1. Selection of control and patient group participants for investigation, execution tonal audiometry, tympanometry, measuring of cortical auditory evoked potentials.
2. Development of language material for speech audiometry.
3. Approbation of language material in the control group.
4. Speech audiometry in the patient group.
5. Electrophysiological investigations – measuring of cortical auditory evoked potentials for the control group and patient group.
6. Medical therapy for 70 patients, using two preparations internally simultaneously – nicergoline 30 mg per day for 90 days and pramiracetam 600 mg per day for 40 days.
7. After medical therapy the participant of patient group investigation repeatedly has investigation of speech audiometry and cortical auditory evoked potentials.

2.1.3. Characteristics of the investigation participant's questionnaire

All data of survey participants are included in questionnaire particularly developed for investigation that is attached in Annex 2 of promotion work. Information about basic parameters of demography and investigation results are summarised in this questionnaire.

2.1.4. Equipment for speech audiometry

Speech material is played by digital disc player (*Sony*, *Model* CDP-497), which is connected with audiometer *Madsen Orbiter 922*. Stimuli were played in audio ear-phones TDH-29. Auditory test took place in particularly provided premises walls of which are processed by sound proof material. Equipment is calibrated according to ISO standards (ISO, 2004).

2.1.5. Equipment and stimuli for CAEP

Equipment. Electric activity of brain during presentation of sound stimuli was registered by *GN Otometrics ICS CHARTER EP* system. It is equipment of electroencephalography type for measuring of auditory evoked potentials, by help of which neurophysiologic response is obtained from head surface electrodes generated by cerebrum to sound stimuli. The sound stimuli were played in ear-phones TDH-29. Cortical auditory evoked potentials were registered from measuring of two channel system, using silver-silver chloride disc electrodes that are fixed by electrode paste on scalp.

We used five electrodes for measuring of cortical auditory evoked potentials. Electrodes were placed on head surface in positions that marked according to international system of electroencephalography electrode location (Jasper, 1958). Electrodes on the head surface were placed in the following positions: active electrodes – in positions Cz or slightly laterally from middle line – in position C2 and C4, the reference electrodes were placed in parotid area – position M1 right side and M2 – left side, but in the bottom part of forehead – in position Fz the ground electrode was placed. Resistance of electrodes was lower than 5 kilo ohms (kOhm). Individual electro-encephalography activity was extended by filter from 100 Hz up to 1000 Hz. CAEP measuring time period was 50 ms before stimuli and 500 ms after beginning of stimuli. For all the electrodes artefacts were excluded by 150 mV filter. Each measurement continued until huge amount (1062) responses free of artefacts were obtained.

Stimuli. Complex signal was made by standard stimuli and different stimuli were rarer between then. Measuring was made when subject was listening actively and passively. When listening actively, the proportion of standard and different stimuli was 9 to 1. Standard stimuli were 25 ms long tones in frequency of 1000 Hz, but different stimuli – 75 ms long tones in frequency of 2000 Hz. Interval between stimuli was 1500 ms Figure (2.1.a). When listening passively, the standard and different stimuli were played in proportion of 8 to 2, they were similar by length – 25 ms. Interval between stimuli was 500 ms. Stimuli were plaid in three sound intensity levels – 65, 70 and 75 dB, masking noise – 60 dB (Figure 2.1.b). Stimuli were played in alternating polarity in order to protect responses from stimuli artefacts as stimuli ended before beginning of response interval.

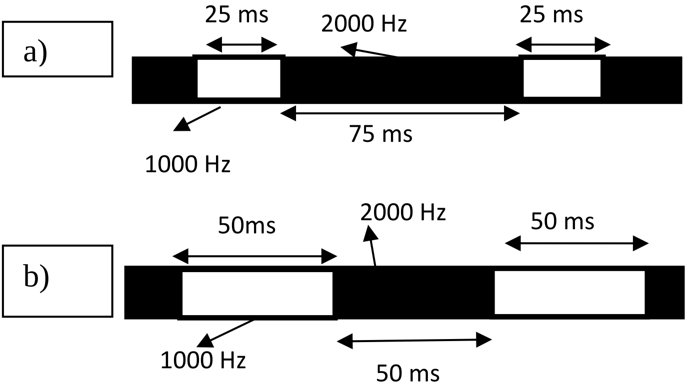


Figure 2.1. Sound stimuli for CAEP listening actively (a) and passively (b)

2.2. Methods

2.2.1. Development of the tests for speech reception threshold

There was no language material in Latvian language for psychoacoustic investigations in speech audiometry. It was established in the beginning part of our work. Establishment of language test could be divided in three stages. In the first stage we selected language material. In the second stage there were made sound recording and then the language material was processed and written in digital form. In the third stage the participants of the investigation control group with normal audition listened to the recorder language material. The language material was selected from large text data basis in the Latvian language. From the former selected 15 000 sentences, 1050 sentences were selected for the further survey on inclusion in speech tests, taking into account several conditions. There were chosen colloquial speech sentences that did not include exclamations, questions, proverbs and they did not include proper nouns and names. Each sentence was made of four to six words. According morphological structure they were extended sentences, syntactically correct, their content – semantically neutral.

The chosen sentences were assessed by the author and work managers together with philology specialists of Artificial Intellect laboratory of Mathematics and informatics institution of the Latvian University. 800 sentences were selected and used for speech test establishment. The language materials were spoken by professional actors, they were requested to speak naturally, with even vocal force, not stressing any of syllables and words. A silence period was kept after each sentence – 10 seconds longer than the time required for text repetition.

The recorded text was listened to by five participants of control group with normal audition in audio ear-phones in comfortable loudness level. The sentences, where any of words was not comprehensible, were excluded, but the other recorded language material – 325 sentences – was kept for the further investigation.

Assessment of sentences equivalency

Subjects. Thirty participants of control group with normal audition participated in assessment of speech material.

Stimuli. Efficiency of language material was assessed for newly made 325 sentences. A wide spectrum of combined white noise of 60 dB was used for signal masking. Comprehensibility of sentences was assessed taking into account the number of correct responses by listening to the signal in both in both ears and the sound in one ear, but noise in the other.

Planning. All the language material was presented to each control group participant (325 sentences). As all the participants received equal stimuli it was possible to compare the replies between subject and sentence sets. Speech reception threshold, with and without masking noise, was determined to each of the participants.

Course of test. Subjects were informed about the procedure course and their assignment, listening to one sentence list as a sample. The subjects listened to the stimuli in ear-phones, afterwards repeated the heard text as precise as possible. In the first part of procedure the sentences were listened in both ears. The first sentence was played in the level of projected reception threshold and afterwards it was lowered by steps until each sentence after it was heard was repeated without mistakes. The correct answers were fixed according to the determined level of speech signal strength in decibels (dB) in graphic picture – audiogram. In the second part of procedure the psychometric function of separate sentences was assessed. During the procedure the speech stimuli was presented in one ear, but masking noise in intensity of 60 dB – in the other. Each sentence was presented only one time. The test was continued until the correct response up to the lowest stimuli sound strength level was obtained. So the speech reception threshold in decibels was determined and fixed in audiogram. The total time required for investigation for one subject was 1.5 hours. Sequence of sentence list listening was similar to all survey subject.

Verification of method. Speech reception threshold was determined, when the subject listened to all 13 test sentences, in total – 325 sentences. After sentence hearing all the sentence words, observing endings had to be repeated loudly. The test was performed in two types. The first test – listening by both ears, the second test – speech signal was played in the right ear and at the same time – masking noise in the left ear. The noise level was constant under the entire test – 60 dB, it had combined white noise of wide spectrum.

Verification of speech reception threshold test sentence selection in the control group. The sentences provided for speech reception threshold test is played in both ears simultaneously. The first three sentences of test list is presented in order to introduce the test procedure and to determine the listening sound strength that is the most comfortable level to the listener. The test is begun from low sound strength – 5 dB. If one or several words are not named correctly, the next sentence is played in the greater noise level, increasing it for 5 dB. The procedure is continued until all the words of sentence are named correctly. All 325 sentences are continued to be presented in this sound strength level. After listening to each sentence, it is marked if all the sentence words are comprehended correctly. The list excludes the sentences, where any word is repeated incorrectly. These sentences are not used in the further tests.

Test of speech reception threshold in noise for the control group. The sentences are begun to be played at level of 5 dB sound strength. The noise level is fixed in level of 60 dB sound strength. The first three test sentences are played in order to introduce the process course to the patient. Afterwards the test is continued by playing ten sentences in each sound strength level. The test is continued, while all words for at least half of 10 sentences (five sentences of 50 % of the sentence list) in any of sound strength level are repeated correctly.

Value of standard deviation of individual speech reception threshold may not exceed 5 dB, or the data on the contrary are considered to be invalid.

In the result the language material for speech reception threshold are made by sentences that are grouped in 12 lists – each of them by 12 sentences. The full test set of sentences – Annex 3.

2.2.2. Development of the dichotic tests

Test of dichotic speech reception is performed by playing different speech stimuli – word in both ears simultaneously. Dichotic speech test (DL) is made, using words in Latvian – one or two syllable nouns grouped in one pair. The word pairs are made by words that have similar syllable syntax. There were made 25 word pairs, for instance, “liepa” (lime) – in left ear, “lapa” (leaf) – in right ear. The words are grouped so that they are semantically different. The numeral word test is made by grouping numeral words in pairs from one to ten.

In dichotic listening tests the stimuli in each ear have to begin and end simultaneously. However, it is advised to present stimulus in one of ears for 15 -–90 milliseconds later than in the other ear, because so precise simultaneous presentation of stimulus in conditions of daily talks would not be adequate, and significantly would reduce the number of correct replies, if the first sound is completely covered.

Taking into account this condition, the stimuli in the right ear in our established test is began to be presented 45 milliseconds later than in the left ear. Each word is recorded separately with similar voice strength and intonation, controlling frequency in professional recording studio, in a particularly equipped room, as well as observing noise level standards (ISO, 2004). 6 seconds long silence pauses are included between the words and are provided for word repetition before playing of each next word (in order to ease the test procedure, the player is not stopped after each word). The number of correct replies without noise for people with good audition was within limits of 90 – 100 %: to signal of woman’s voice – 90 %, to signal of man’s voice – 100 %. Wrong replies were tested repeatedly. The words that were not comprehended correctly by people with good audition were taken out of the list. The prepared language material is recorded in compact disc (CD) for practical usage.

Process of dichotic speech reception test. Before dichotic speech recognition test investigation the participants were introduced to dichotic listening task – each was read the instruction about test process. The word pair was played in the ear-phones of the subject – different word in each ear at the same time and afterwards the subject repeated both of the words in loud voice, but we registered the correct replies in audiometer. At the end of test the number of correct replies as well as percentage of the number of correct replies from the total number of word pairs was registered in the minutes. Then the next word pair was played. In order to be sure about the reliability of the results, the playing was began by 20 dB, increasing the sound strength for 10 dB, until the most comfortable listening sound strength to participants of control group with normal audition was reached – 55 dB. Measuring of dichotic word and digit word reception was made in such sound strength. The participants of control group correctly perceived 95 % of dichotic word test words and 100 % of numeral word test words.

Reception of dichotic words was determined by usage of free responding type, i.e., calling all the head words. All 25 word pairs of dichotic word test (DV) and 16 digit word pairs of dichotic digit word test (DC) were played to each subject in comfortable listening conditions. All dichotic word pairs were played in 55 dB sound level. When dichotic word pair was played, the subject loudly spoke the words heard in both ears and they were fixed as correct or incorrect reply. The subjects were advised to listen as attentive as possible and reply correctly. Similar word list was played to all subjects so that the results were comparative.

2.2.3. Procedure of determination of the speech reception threshold

Stimuli. For speech reception threshold determination the sentence tests in two listening types established in the investigation were used. In the first stage the speech material was played in both ears. In the second stage the speech stimuli was played in the right ear, but noise – in the left ear.

Assessment of speech reception threshold results. Sentences were played in both ears simultaneously. The first three sentences of the test list were presented in order to introduce the test course. The test is started from a small sound level – 10 dB. If one or several words are not named correctly, the next sentence is played in the greater sound strength, increasing it for 5 dB. The test is continued until all sentence words are named correctly in at least 50 % volume, i.e., in five sentences from ten in any of the tested level of sound strength. This level of sound strength is considered the threshold of speech reception. Threshold of speech reception is level of sound strength, where at least in five of ten sentences played in ears all the sentence words are repeated correctly, observing the word endings.

Speech reception threshold in noise. The test is performed by playing the speech signal (sentence) in the right ear simultaneously with masking noise in the left ear. The sentences are started to be played in 5 dB sound strength level, the noise – in 60 dB sound strength level. The test is continued, while all words to at least five (50 % of test material) from ten sentences in any of sound strength level. Speech reception threshold in noise is sound strength level, in which at least five (50 %) of ten test sentences in the right ear – simultaneously with masking noise in the left ear – all words of the sentence are repeated correctly, observing word endings.

2.2.4. Procedure of the determination of the dichotic speech

Before test the survey participants were introduced to dichotic listening assignment – instruction for procedure course was read to each subject. Afterwards the test listening was performed by listening to three word pairs. Different sound stimuli were played in each ear simultaneously in dichotic reception test. After simultaneous playing of word pairs (one of pair words in the right ear, the other word – in the left ear) the subject has to repeat both heard words. The correct replies from each ear were fixed in audiometer. Then the next word pair was played from ten test word pairs (in total 16 word pairs, three of them – control word pairs).

All dichotic word pairs are played in sound intensity level of 55 dB that complies with comfortable audition sense. After dichotic word pair is played, the subject has to speak out loudly words that are heard in both ears. The correct replies from each ear were counted. Equal word list was played to all subjects so that the results are comparable. Result of dichotic test is expressed in percent by calculating the correctly identified word number against the word number presented in both ears. Prevalence of right ear dichotic speech reception in comparison with the one calculated for left ear in percent, assuming the number of correct replies from the right ear as 100 %.

2.2.5. Procedure of recording of central auditory evoked potentials

The patient is in comfortable reclining position, backing the head, with electrodes places on scalp and with ear-phones. During passive listening in order not to turn attention to sound stimuli, the subject is requested to read magazine, during active listening – to count different stimuli. CAEP was performed in three sound stimuli intensities, each of them – three measuring, when listening actively and three – when listening passively. The first measuring session – listening actively, and then break of 10 minutes, afterwards – measuring – listening passively. The length of procedure is individual – 2 – 2.5 hours.

2.2.6. Analyses of central auditory evoked potential curves

For each of investigation procedure parameters three measuring were made in order to assess the homogeneity. When assessing each measuring pair, we identified components of cortical auditory evoked potentials P1, N1, P2, N2 and P3 on electrophysiological response curve, if its amplitude differs from the basic line for 1 millivolt (μV) and more, taking into account that planned localisation of this component on curve. Wave amplitude is identified by average amplitude in basic line in 50 ms interval before beginning of stimuli.

2.2.7. Medical therapy

Participants of patient group internally used two pharmaco-preparations – nicergoline 30 mg once per day for 90 days and pramiracetam 600 mg one per day for 40 days. After medical therapy course, i.e. after three months speech audiometry and measuring of cortical auditory evoked potentials are performed repeatedly after three months according the former described methods. The obtained results are analysed in comparison with survey results before medical therapy.

2.2.8. Statistical methods used in the study

Purpose of data statistical analysis was to assess the audition differences for people with normal audition and patients with auditory disorders according to respective statistical methods. By variable size the parameter of central tendency was calculated – mean arithmetic value of the mark, median and mode as well as variance parameters – standard deviation, minimal and maximal value of the mark. In order to determine if data comply with normal distribution, there was used Shapiro – Wilk test. For comparison of two dependant and independent groups by one sign there is used complying Student *t* test, but for comparison of several independent groups by one sign – variance analysis.

Threshold of statistic credibility for results of double-sided tests is considered to be *p* value < 0.05. Fisher *LSD post-hoc* statistical analysis method is used in order to determine differences of some parameter to any of the survey groups in comparison with other survey groups. In cases when the analysable data do not comply with normal division, the appropriate non-parametric test is used – Mann–Whitney, Wilcoxon or Friedman. The results were assessed as statistically credible different, if probability of zero hypotheses was 0.05 or lower, i.e. criteria for zero hypothesis refusal was materiality level of p=0.05. Otherwise there was accepted zero hypothesis. For analysis of two mark connection there is used Spearman coefficient correlation analysis and Pierson correlation analysis. The following correlation for continuity classification by correlation coefficient *r* size is assumed in this investigation:

- Correlation is weak, if $r \leq 0.3$;
- Correlation is average, if $0,3 < r < 0.7$;
- Correlation is tough, if $r \geq 0.7$.

Connection between two parameters was searched also by linear regression method. When analysing nominal or range data, there was used Pearson Chi square statistical analysis, if frequency of contingence table was less than 5, but Fisher precise test was used, if frequency of contingence table was greater than 5. For determination of two comparative groups border values there were used ROC curves and this method of statistical analysis provided information about sensitivity and specificity of two features data division border value. Area below the curve is used for comparison of border value quality. Analysis of biserial coefficient was used assuming such assessment of statistical effect:

- small, if $r < 0.1$;
- mean, if $0.1 < r < 0.5$;
- large, if $r > 0.5$.

So that the results could be generalized and the variance limits could be determined, there was also calculated 95 % of credibility interval value.

In this study, the software package *SPSS "Statistical Package for the Social Sciences", version 20.0 for Windows*, was used for statistical analysis of data and presentation of the research results.

3. RESULTS

3.1. Developed tests for speech audiometry

The developed language material for speech reception threshold determination consists of sentences that are grouped in 12 lists – 12 sentences per each.

Dichotic word test (DV) and dichotic numeral word test (DC) in the Latvian language was developed for assessment of dichotic reception.

3.2. Results of speech audiometry

3.2.1. Speech reception threshold

Table 3.1. summarises speech reception threshold (RUS) and speech reception threshold in noise (RUS/T), mean indices for control group (N), young (JPG) and elder patient groups (VPG).

Table 3.1.

Mean values an standard deviations for speech reception threshold in noise (RUS/T) and quite (RUS)

Investigation group		RUS	RUS/T
N	Mean value, dB	18.28	20.86
	Standard deviation	2.42	1.92
JPG	Mean value, dB	42.36	47.43
	Standard deviation	7.07	6.73
VPG	Mean value, dB	43.18	49.24
	Standard deviation	7.27	5.61

The mean values for speech reception threshold in noise (RUS/T) and without noise (in quite) (RUS) differed statistically credibly in all the groups (F (2.96) = 161.49; $p < 0.001$). Variance analysis ANOVA showed that the mean values for speech reception threshold in noise (RUS/T; $p < 0.001$) and without noise (RUS; $p < 0.001$) differed statistically credibly in all the groups of investigation participants. The control group had significantly smaller difference between speech reception threshold and speech reception threshold in noise ($p < 0.001$).

3.2.2. Dichotic speech reception

Results of dichotic numeral words (DC) and word (DV) tests (the correct replies in percent) for right and left ear, as well as prevalence of right ear in percent are summarised in Table 3.2. (for control group), Table 3.3. (for JPG) and Table 3.4. (for VPG). In DV test the number of right answers in comparison with DC test statistically more credibly reduced in both groups of patients ($p < 0.001$), but in control group – only for some individuals, that did not affect the group results significantly.

Table 3.2.

The correct replies and SD (in percent) of dichotic numeral words (DC) and words (DV) tests for right and left ear and prevalence of right ear for control group

Dichotic test Investigated ear	DC test Right ear	DC test Left ear	DV test Right ear	DV test Left ear
Correct replies (%)	97.24	90.34	97.24	90.34
Standard deviation (%)	2.53	5.96	2.53	5.96
Prevalence of right ear (%)	8.01	–	8.21	–

Table 3.3.

The correct replies and SD (in percent) of dichotic numeral words (DC) and words (DV) tests for right and left ear and prevalence of right ear for young patient group

Dichotic test Investigated ear	DC test Right ear	DC test Left ear	DV test Right ear	DV test Left ear
Correct replies (%)	69.19	54.72	62.70	47.36
Standard deviation (%)	5.95	6.20	7.22	6.26
Prevalence of right ear (%)	21.1	–	25.47	–

Table 3.4.

The correct replies and SD (in percent) of dichotic numeral words (DC) and words (DV) tests for right and left ear and prevalence of right ear for elder patient group

Dichotic test Investigated ear	DC tests Right ear	DC tests Left ear	DV tests Rihgt ear	DV tests Left ear
Correct replies (%)	67.73	55.15	61.82	47.27
Standard deviation (%)	7.08	6.31	7.78	5.87
Prevalence of right ear (%)	19.57	–	24.53	–

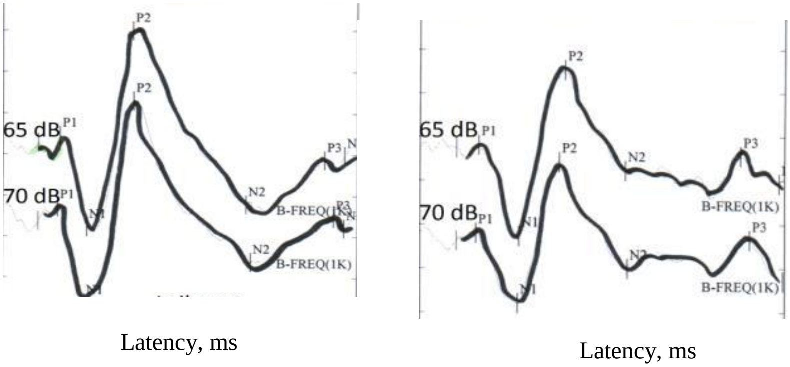
Difference between speech reception in the right and left ear was stated in both dichotic speech reception tests that in DV test were seen more significantly than in DC test. It was testified by the greater number of correct replies from the right ear than from the left ear in all the investigation groups ($p < 0,001$).

After analysis of Pearson correlation coefficient we concluded that there is not statistically credible correlation between DC reception in the right and left ear for JPG and VPG subjects that testified about prevalence of right ear reception, besides prevalence of the right ear in DV test is greater than in DC test ($r = 0.79$; $p < 0.001$). For VPG and JPG the difference between the ability of right and left ear speech reception exists, and also prevalence of the right ear over the left ear in dichotic speech tests is greater ($r = 0.66$; $p < 0.001$).

3.3. Results of electrophysiological investigation

3.3.1. CAEP latencies and amplitudes

Central auditory structure modulating cortical auditory evoked potentials components in curve of electrophysiological response is representing beginning from 50 s after stimuli beginning. When listening passively, CAEP component N1, P2 and N2 amplitude was 1.5–2.5 μV, but P3 amplitude is smaller than 1 μV. In its turn, when listening actively, component P3 on electrophysiological response curve was registered with greater amplitude (> 1.5 μV), but amplitudes of components N1, P2 and N2 did not change significantly (Figure 3.1.).



a) **b)**

Figure 3.1. Cortical auditory evoked potential waveforms for young patient group subject listening passively (a) and actively (b)

The mean values for the investigation groups in each CAEP component latency in three different sound intensity levels (65, 70, 75 dB) and standard deviations are summarised in tables (for component P1 – in Table 3.5., for component N1 – in Table 3.6.).

When increasing signal intensity, CAEP component P1, N1, P2 and N2 latencies were significantly reduced in comparison with mean latencies of component P3. Besides most of all mean values of components P1, N1, P2 and N2 latencies reduced in both groups of patients and exactly in group of elderly patients ($p < 0.005$).

Table 3.5.

Mean values and standard deviations of peak latencies (ms) of CAEP component P1 responses in condition of 65, 70 and 75 dB stimuli intensities for controles participants (N), young (JPG) and elderly patient groups (VPG)

Group	Investigation group		P1 65 dB	P1 70 dB	P1 75 dB
Controles	N	Mean value	64.48	60.45	56.39
		Standard deviation	5.04	4.06	5.01
Patients	JPG	Mean value	75.66	67.77	60.65
		Standard deviation	6.28	6.47	5.67
	VPG	Mean value	74.33	68.32	62.92
		Standard deviation	8.51	8.16	8.11

Table 3.6.

Mean values and standard deviations of peak latencies (ms) of CAEP component N1 responses in condition of 65, 70 and 75 dB stimuli intensities for controles participants (N), young (JPG) and elderly patient groups (VPG)

Group	Investigation group		N1 65 dB	N1 70 dB	N1 75 dB
Controles	N	Mean value	83.24	78.47	73.32
		Standard deviation	5.05	3.75	2.80
Patients	JPG	Mean value	111.11	95.78	85.78
		Standard deviation	13.56	9.23	8.01
	VPG	Mean value	103.69	93.58	85.21
		Standard deviation	14.32	11.34	9.88

Increase of signal intensity impacted latency of component P3 the least. Increasing stimuli intensity, mean value of component P3 latency statistically credibly does not change for patients of young age — no 359.89 ms 65 dB signal intensity level up to 337.57 ms in level of 75 dB ($p < 0.001$) and for subjects of control group (from 293.35 ms in 65 dB signal intensity level up to

282.86 ms in level of 75 dB ($p < 0.001$)), in its turn mean value of P3 latency in elderly patient group reduced statistically credibly – from 354.55 ms in 65 dB signal intensity level up to 322.78 ms in 75 dB level ($p < 0.001$).

After variance analysis (ANOVA) we concluded that component P1 average latency between all investigation groups differ statistically credibly (F(2.96) = 13.87; $p < 0.001$) and mean value of component N1 latency for all investigation groups differ statistically credibly (F(2.96) = 34.97; $p < 0.001$).

Using LSD *Post-hoc* analysis we concluded that latency of component P1 for control group differ from JPG and VPG statistically credibly ($p < 0.001$), but JPG from VPG does not differ statistically credibly ($p = 0.72$).

Component latencies of cortical auditory evoked potentials, receiving signal in noise

Statistical analysis of data showed that under impact of noise all the components do not change equally and that changes between survey groups differ although CAEP component latencies extended for all the components.

CAEP component latencies P1 and N1 extend, when the signal is received in noise. Mean latency of component P1 in noise among all the survey groups differ statistically credibly (F(2.95) = 11.94; $p < 0.001$).

Using LSD *Post-hoc* analysis, we concluded that latency of component P1 in noise for control group (N) from young patient group (JPG) and elderly patient group (VPG) differ statistically credibly ($p < 0.001$), but JPG does not differ from VPG statistically credibly ($p = 0.54$): for control group it was significantly smaller than for both patient groups, but noise extended latency of P1 similarly for both patient groups.

Variance analysis showed that the mean values for latency of component N1 in noise for all the investigation groups differ statistically credibly (F (2.95) = 10.63; $p < 0.001$). Using LSD *Post-hoc* analysis, in order to determine differences between groups we concluded that latency of component N1 differ from JPG and VPG statistically credibly ($p < 0.001$), but JPG does not differ from VPG statistically credibly ($p = 0.30$). Using LSD *Post-hoc* analysis, we concluded that latency of component N1 in noise for control group differs from young and elderly patient group statistically credibly ($p < 0.001$), but JPG does not differ from VPG statistically credibly ($p = 0.89$): for control group it was significantly smaller than for both patient groups, but noise extended latency of N1 similarly for both patient groups. According variance analysis (ANOVA) we concluded that mean value of component P2 latency for all the investigation groups differ statistically credibly (F(2.96) = 10.41; $p < 0.001$), also mean value of component P2T latency in noise for all the investigation groups differ statistically credibly (F(2.95) = 12.26; $p < 0.001$).

Using LSD *Post-hoc* analysis, in order to determine differences between groups we concluded that latency of component P2 for N group differ for JPG and VPG statistically credibly ($p < 0.001$), but JPG does not differ from VPG statistically credibly ($p = 0.47$). The results testify that noise essentially extends latency of component P2 in all the survey groups, but largely and similarly – in both patient groups.

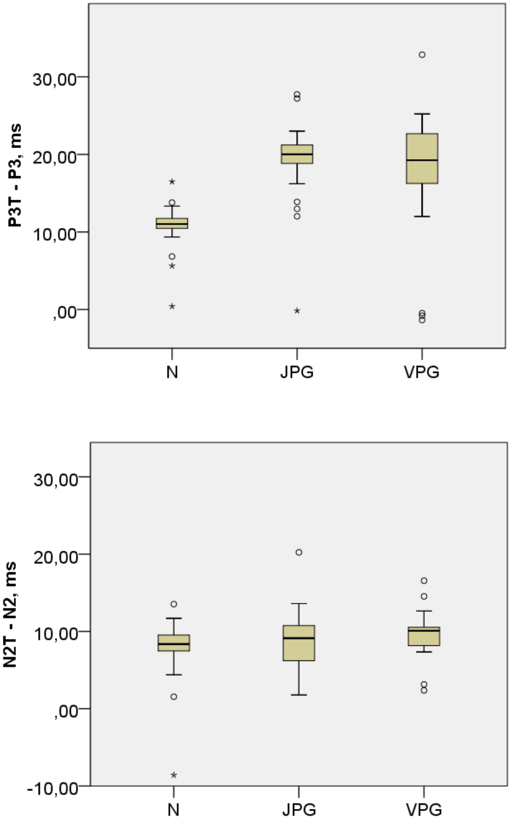
According variance analysis (ANOVA) we concluded that mean value of component N2 latency for all the investigation groups differ statistically credibly ($F(2.96) = 62.42$; $p < 0.001$), as well as mean value of component N2 latency in noise for all the investigation groups differ statistically credibly ($F(2.95) = 6.86$; $p < 0.001$).

Using LSD *Post-hoc* analysis, we concluded that N2 latency, when listening the signal in noise and without noise for control group (N) differed statistically credibly ($p<0.001$) from the young patient group (JPG) and elderly patient group (VPG), but mutually JPG and VPG does not differ statistically credibly ($p=0.47$). Noise essentially extends latency of component N2 in all the survey groups, but largely and similarly – in both patient groups (Figure 3.2.a).

CAEP component P3 latency at signal in noise is extended for both patient groups and control group. In comparison with other components, the noise impacted latency of component P3 most significantly. According variance analysis (ANOVA) we concluded that mean value of component P3 latency for all the investigation groups differ statistically credibly ($F(2.96) = 113.35$; $p < 0.001$). Also by variance analysis (ANOVA) we concluded that mean value of difference of component P3 latency receiving signal in noise (P3T) and without noise for all the investigation groups differ statistically credibly ($F(2.95) = 137.18$; $p < 0.001$) (Figure 3.2.b).

Using LSD *Post-hoc* analysis, in order to determine group differences we concluded that P3 latency for control group (N) differed statistically credibly ($p<0.001$) from the young patient group (JPG) and elderly patient group (VPG), besides P3 latencies for JPG differed statistically credibly also from VPG ($p=0.04$).

Using LSD *Post-hoc* analysis, in order to determine group differences we concluded that P3 latency in noise for control group (N) differed statistically credibly ($p<0.001$) from the JPG and VPG, but mutually JPG and VPG does not differ statistically credibly ($p=0.08$).



Investigation group Investigation group

a) **b)**

Figure 3.2. Group differences for latencies of CAEP component N2 (a) and P3 (b) in noise and quite

Control group **Patients (JPG+VPG)**

3.3.2. Limit values of CAEP components

ROC curves are used for determination of limit values of cortical auditory evoked potentials components in control group and patient group.

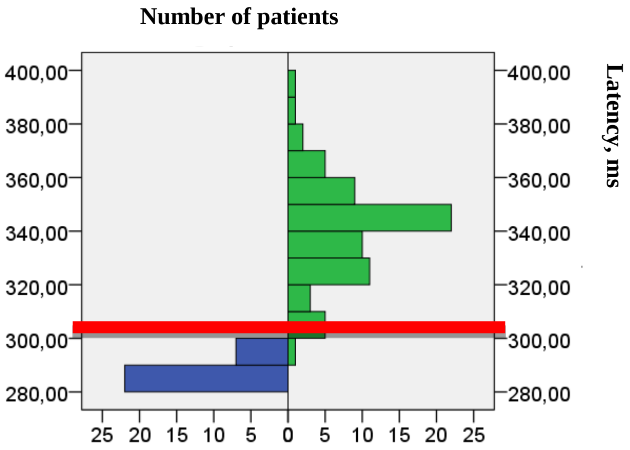


Figure 3.3. Limit value of cortical auditory evoked potentials component P3 in control group and patient group

Analysis of our survey results showed that most sensitive CAEP measuring is latency of component P3. According ROC curve analysis we concluded that P3 limit value for control group and both patient groups is 304.77 ms at 95 % sensitivity and 99 % specificity (Figure 3.3), but are below curve AUC = 0.99 ($p < 0.001$).

The second more sensitive measuring by ROC curve analysis was component N2 latency, border limit of which both for control group and both patient groups is 220.23 ms at 90 % sensitivity and 98 % specificity, the area below curve AUC = 0.81 (p < 0.001) (Figure 3.4).

ROC curve analysis showed that P1 border limit for control group and both patient groups is 64.8 ms at 62 % sensitivity and 90 % specificity area below curve AUD = 0.81 ($p < 0{,}001$). By analysis of ROC curve we concluded that limit value of component N1 for control group and patients is 82.06 ms at 88 % sensitivity and 73 % specificity, area below curve AUC = 0.93 ($p < 0{,}001$), limit value of component P2 for control group and both patient groups is 138.66 ms at 61 % sensitivity and 90 % specificity, area below curve AUC = 0.80 ($p < 0{,}001$).

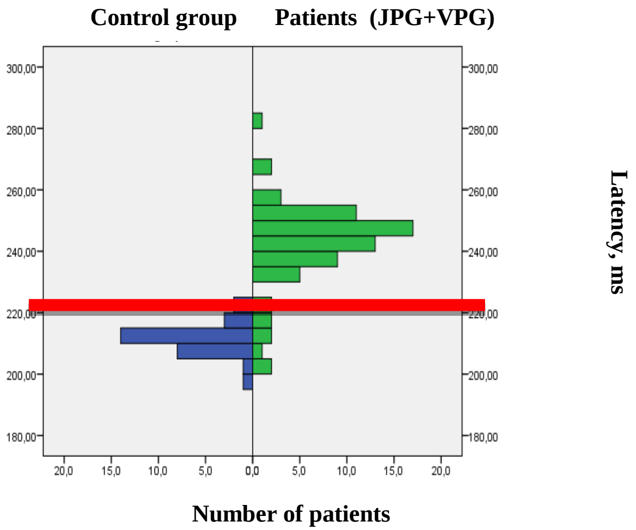
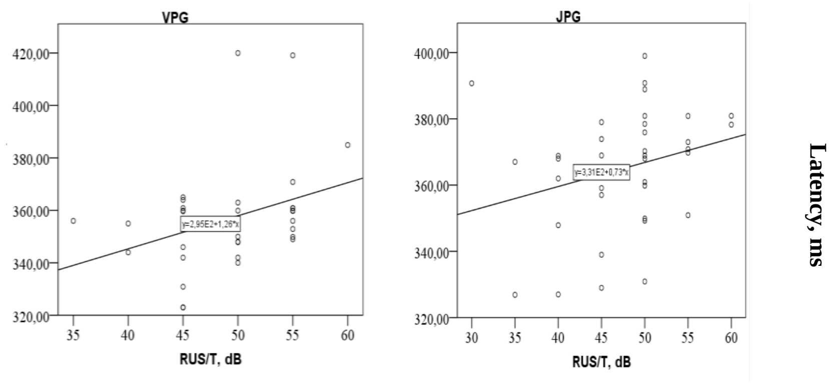


Figure 3.4. Limit value of cortical auditory evoked potentials component N2 in control group and patient group (marked with red horizontal line)

3.3.3. Correlations between speech audiometry results and CAEP latencies

Association between cortical auditory evoked potentials components P1, N1, P2, N2 and P3 latencies, speech recognition threshold and dichotic test mean values was assessed by usage of Spearman coefficient correlation analysis. There were analysed 24 correlations, whereof six were positive. Spearman coefficient correlation analyses showed mean tight and statistically credible correlation between latency of component P3 and speech reception threshold (RUS) ($r_s = 0.35$; $p < 0.05$) in control group.

By Spearman correlation coefficient analysis we concluded that between speech reception threshold in noise (RUS) and CAEP component P3 latency in noise there are statistically credible correlation for elder patient group ($r_s = 0,35$; $p < 0,05$) and young patient group ($r_s = 0.36$; $p < 0.001$) (Figure 3.5).



a) b)

Figure 3.5. Association between latency of cortical auditory evoked potentials component P3 and value of speech reception threshold in noise (RUS/T) in elderly (a) and young patient group (b)

After Pearson correlation coefficient analysis we concluded that between dichotic word reception (DV) and component P3 latency in noise (P3T) there is no statistically credible correlation ($p = 0.34$) in young patient group. Spearman correlation coefficient analysis showed that there is no statistically credible correlation ($p = 0.60$) between dichotic word test (DV) and component P3 latency in noise (P3T) for elder patient group. In this case non-existence of statistically credible correlation testifies about clinically positive deposit.

3.4. Speech audiometry after medical treatment

When using *t*-test analysis of dependant selections, we concluded that number of correct replies for dichotic word test (DV) and dichotic digit word test (DC) for both patient groups after therapy increased statistically credibly ($p < 0,001$).

Although dichotic speech perception by the right ear in comparison with the left ear after therapy for both patient groups was maintained statistically better credible ($p < 0.001$) dichotic numeral word test in comparison to the result in dichotic word test, the prevalence of right ear reception after therapy reduced.

According to biserial coefficient analysis (Figure 3.6) it is concluded that in both patient groups dichotic digit word recognition after therapy significantly improved by left ear and right ear – the difference of results between number of correctly heard words was high both for the left ear

(DCKM-DCK; (r = 0.80; $p < 0.001$)), and for right ear (DCL and DCLM-DCL; (r = 0.54; $p < 0.001$)).

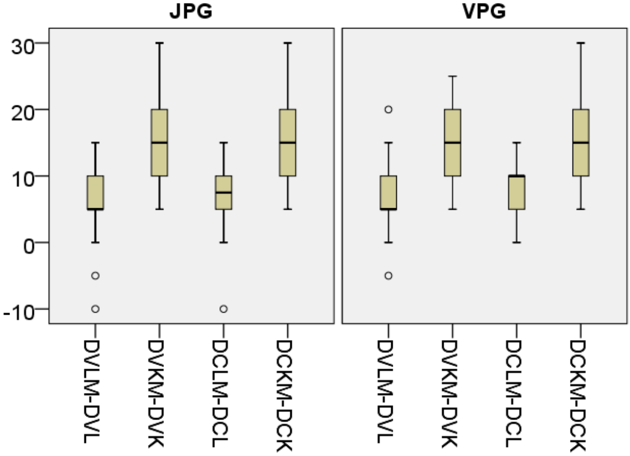


Figure 3.6. Dichotic recepion for right and left ear before therapy in DC test un DV test and after therapy in DC test (DC M) un DV test (DV M) in young (JPG) and elder patient groups (VPG)

According to biserial coefficient analysis it is concluded that in both patient groups dichotic digit word reception after therapy significantly improved for both ears – the high difference between number of correctly heard words was stated for both the left ear (DCKM-DVK; (r = 0.52; $p < 0.001$)) and for right ear (DCLM-DVL; (r = 0.76; $p < 0.001$)).

3.5. CAEP latencies after medical treatment

After medical therapy latencies of cortical auditory evoked potentials (CAEP) components P1, N1 and P2 reduced in young patient group and elder patient group ($p < 0{,}001$). Dynamics of CAEP components latencies after therapy is similar in all sound intensity levels (Table 3.7.).

According variance analysis (ANOVA) we concluded that mean latency of component P3 after therapy (P3 M) in comparison with latency before therapy (P3) shortened statistically credibly both for young patient group (F = 33.40; $p < 0.001$) and elder patient group (F = 2.64; $p = 0.04$).

Table 3.7.

Mean values and standard deviations of peak latencies (ms) of CAEP components before (P1, N1, P2, P3) and after medical therapy (N1M, P1M, P2M, P3M) for control group (N), young (JPG) and elderly patient groups (VPG)

Investigation group		N1	N1M	P1	P1 M	P2	P2 M	P3	P3 M
JPG	Mean value (ms)	95.78	85.08	67.77	59.88	141.08	130.08	344.60	342.87
	Standard deviation	9.23	7.82	6.47	3.87	7.92	4.61	19.71	19.89
VPG	Mean value (ms)	93.58	86.71	68.32	58.94	142.51	130.42	336.84	332.33
	Standard deviation	11.34	8.17	8.16	5.73	10.36	6.45	18.02	16.76

4. DISCUSSION

Long-term survey is reflected in the promotion work – psychoacoustic and electrophysiological investigations are executed during more than five years. In the beginning stage there was performed speech audiometry and started investigations of auditory evoked potentials to people with normal audition. When getting more experience, we improved the methods and afterwards executed measuring to people with auditory disorders.

Patent (LV14096) developed by us was registered for central auditory processing assessment in Latvia.

4.1. Speech audiometry

4.1.1. Speech reception threshold

Psychoacoustic method – speech audiometry – that was used for more than several tenths of years is maintained as principal method for central auditory assessment (Broadbent, 1954; Jerger, 1998; Keith 1995; Musiek et al., 1983; Cameron et al., 2011).

We used speech form that is characteristic to daily colloquial language in tests of speech reception threshold (Brown et al., 2010), using sentences (Divenyil et al., 2005; Cameron & Dillon, 2007a).

Within this investigation, speech audiometry tests were made so that the results are assessable and comparable, taking into account the international experience (Plomp, 1976; Nilsson, 1994; Lee & Humes, 1993; Cameron & Dillon, 2008). It is important to numerically small nation languages, because there tests will be used for small groups of people.

It is possible to assess the central auditory processing as precise as possible, modulating conditions of listening (Gelfand et al., 1988; Helfer & Freyman, 2008), therefore reception measuring were performed also in masking noise. In order to avoid inaccuracy measuring and thus in the result assessment masking noise was played in fixed sound strength level of 60 dB, because psychoacoustic method procedure impacts the accuracy of test results. Thus our results were similar to works of other authors (Nilsson et al., 1994; Harris et al., 2009).

In our survey we determined that speech reception threshold was higher in young patient group and elder patient group (respectively 42.36 dB, SD = 7.07 and 43.18 dB, SD = 7.27) in comparison with the control group (18.28 dB, SD = 2.42).

Determining speech reception threshold (RUS) in noise, for the control group it increased insignificantly (20.86 dB, SD = 1.92) in comparison with RUS without noise. In the contrary RUS noise statistically credibly increased for young patient group (47.43 dB, SD = 6.73) and elder patient group (49.24 dB, SD = 5.61) that verifies about central auditory disorders.

Central auditory processing is deeply characterised by difference between speech reception threshold without noise and in masking noise (Moore, 2006; Cameron & Dillon, 2007b).

In the control group the difference of speech reception threshold in noise and without noise (S/T) was 2.59 dB (SD = 3.44). Similar S/T value was given by Swedish HINT, where mean S/T was 3.0 dB with standard deviation 1.1 dB (Hällgren et al., 2001), and American English HINT, where mean S/T was 2.9 dB with standard deviation of 0.78 dB (Nillsson et al., 1994).

Speech reception threshold in noise and without noise in people group with audition disorders correlate with Hagerman (1982) survey (8.1 dB) and Cameroon *et al.* (2005) (6.2 dB) investigation results.

Tough correlation between decrease of high frequencies sensorineural audition and speech reception threshold is not found and it indicates that meaning is not only to process of audition decrease related to ageing (Yonan & Sommers, 2000; Pilotti et al., 2001; Pilotti & Beyer, 2002). It was approved also in our investigation – in our investigation speech reception in noise was reduced also for participants of young patient group.

4.1.2. Dichotic speech reception characteristics

In our world we established also dichotic word and digit word tests in Latvian that are adapted by similar method in English (Broadbent, 1954; Musiek, 1983). Linguistically different word tests of two types were used in order to determine cognitive aspect, assessing impact of speech stimuli in central audition process.

Dichotic tests by test results of control group subject with good audition were established so that they are easy to assess. Results of control group comply with normal dichotic speech reception. Small prevalence of the right ear was considered normal audition processing corresponding to anatomy of audition track and physiology (Kimura, 2011).

In our survey we concluded that properties of audition dichotic stimuli impact speech reception results. Reception of dichotic digit word for subjects of the control group was high, but the results in the patient groups were significantly weaker.

Results of our survey dichotic tests verify about significantly reduced central auditory processing for patient groups in comparison with the control group that is similar to *Musiek* (1983) and *Kimura* (2011) results that consider dichotic speech reception tests the most intensive in diagnostics of central audition deficit. *Musiek & Chermak* (2007) recommends dichotic speech reception tests as obligatory part of central audition processing assessment.

The results of our survey marked two main deposits. In both patient groups dichotic reception was weaker in comparison with the control group. Statistically more credibly greater number of correct replies is to the right ear in all investigation groups. This proportion remained for both linguistically different dichotic test types. The correctly heard word number was greater in digit word test in comparison with word test in all investigation groups. These results testify that dichotic reception abilities essentially are impacted also by dichotic stimuli linguistic content.

Binaural audition disorders are considered to be symptom of significant central audition dysfunction, origin of which is related to changes in signal analysis process in central auditory segment (Hällgren et al., 2001; Freigang et al., 2011). Also Roup *et al.* (2006), used dichotic word reception tests, concluded that prevalence of the right ear for people with audition disorder is greater (mean 22 %) in comparison with young people with good audition (mean 9 %) that complies with our investigation results. Cognitive abilities that are related to the language material used in it are required in dichotic tests. Also *Hällgren et al*. (2001) considers that complicity of acoustic signal properties impacts reception. Results of our investigation showed that audition disorder affects both young and elderly patients. It shows that signal transmission disorder between hemispheres is not related only to functional changes caused by ageing.

Methods of audition psychoacoustic investigation has limitation, because speech perception impacts cognitive and language factors. In order to reduce their impact to audition test results, we surveyed central audition process in electrophysiological aspect, using cortical auditory evoked potentials, analysed correlations between psychoacoustic tests and cortical auditory evoked potentials.

4.2. Cortical auditory evoked potentials

4.2.1. Effect of stimulus features on CAEP latencies

In our survey we established diagnostically informative cortical auditory evoked potentials measuring procedure. It is possible to investigate audition function by electrophysiological method more selectively, reducing subjective factors in comparison with speech audiometry, results of which is impacted by structures involved in audition function together with cognitive function.

Important advantage of CAEP method is signal perception in the way of passive listening – without attention signal in ear-phones that reduces impact of subjective factors (motivation, memory).

Early CAEP components P1, N1, P2 and N2 are not impacted by attention (Näätanen, 1999, 2009), therefore measuring are executed in passive type of listening – without attention to signals that exclude selective attention and reduces impact of cognitive function.

Increasing intensity level of stimulus, CAEP component P1, N1, P2, N2 latencies shortened, when listening to signal without masking noise (Martin & Stapells, 2005).

Negative component N1 is dominating in electrophysiological response curve of cortical auditory evoked potentials that reflect sensitivity in presence of acoustic irritant (Hyde, 1997; Näätanen & Picton, 1987). Our results approve that latency of component N1 is most sensitive to changes of stimulus intensity. N1 latency significantly shortened increasing stimuli intensity that is similar to *Näätanen & Winkler* (1999), *Bell et al.* (2010), *Billings et al.* (2011) results that consider N1 component as important indicator to the fact that sound signal is received in central nervous system.

Our survey component N1 as well as component P2 amplitude was high and similar to finding in surveys to adults who used complex tone stimuli (Eëponienė et al., 2008).

In our survey CAEP early component P1, N1, P2 latency control group differed from both patient groups for which it was longer, besides mutually smaller difference was between young patient group and elder patient group. Latencies of these CAEP components for elder patients were longer than for the younger patients.

Amplitude of component N2 together with age reduced, but in active paradigm N2 amplitude increased (Näätanen & Picton, 1987). N2 amplitude reduction in adult age is related to the increase of following positive component P3 amplitude by years.

Similar results are obtained using low frequency tonal stimuli that causes greater amplitudes of N1 and P2 components that the high frequency tones (Harris et al., 2008). Low frequency sound better activates sublimis part of cortex and causes greater amplitude in cortex respond that high frequency sounds, using electrodes on scalp surface. However signal frequency is not the only factor that impacts CAEP component amplitude. Component P1 amplitude for adults usually is low. It is followed by negative polarity component N1 of great amplitudes. It is explained by P1 phase ending before negative N1 (Ponton et al., 2002).

Amplitude of component N1 does not changes significantly by the age, but it is generated by high amplitude in different electrode localisation on scalp in different ages (Mueller et al., 2008). Stimulus reception and identification just like as N1 reflect component P2 (Eëponiene et al., 2008). Components P2 and N2 generate more latterly from central line, by increase of age (Raz, 2005). For elderly people who do not complain about audition disorders, latencies of component N1 and P2 does not essentially differ from young adults with good audition (Sörös et al., 2009; Pekkonen et al., 1995). It indicates that ageing does not obligatory associate with evoked potential N1 and P2 extended response, particularly if there are no subjective claims about auditory disorders. In our investigation N1 and P2 latency values were greater for both groups of patients in comparison with control group subjects. It verifies that CAEP component N1 and P2 delayed latencies indicated disorders in central auditory processing that is approved by other surveys (Martin & Stapells, 2005; Sussman et al., 2006).

At complex stimuli, when listening in passive way, cortical auditory evoked potentials latencies between groups differ. In its turn reception of active and passive sounds and discrimination for adults in different ages is similar and it is verified by similar changes of component P1, N1 and P2 latencies (Kujala et al., 2007). Component N2 is less surveyed and it does not have great significance. In our investigation N2 was component of negative amplitude (about 2 μV), the latency of which was significantly extended by noise. N2 amplitude was increased by active listening just like to component P3. By repeated measuring, amplitudes of potential waves caused by equal intensity stimulus were lower than in the first measuring with identic stimulus. It is explained by sensory barrier, due to which a weaker response was generated to the next stimulus, showing atypical waves and waves of lower amplitude and neurophysiological mechanisms that are responsible for delay of information flow (He et al., 2008).

Results testify that curve morphology is significantly impacted by noise, but less by stimulus intensity. Properties of separate CAEP component latencies signal are impacted differently. Latencies of early component P1, N1, P2 and N2 are extended by signal intensity more than by noise. Although all CAEP component latencies were extended, the least noise was impacted by P1, but mostly – by P3. The greatest impact of noise extending P3 latency was in patient groups and mostly in young patient group.

Our results show that in masking noise, when signal is competing with noise, the latencies of cortical auditory evoked potentials are extending and they reflect activity of cortex neuron population to stimulus change. It testifies that auditory disorders in these cases are more impacted by signal and noise relation than the intensity level of stimulus (Billings et al., 2009).

Our results verify that CAEP component latencies and amplitudes were impacted by stimuli properties – sound signal intensity and frequency as well as attention to stimulus, masking noise and location of electrodes on scalp.

4.2.2. Characteristics of CAEP component P3

CAEP component P3 morphology by response to sound signal differed for participants of our investigation groups – control group of people with good audition and both patient groups.

Measuring of P3 CAEP component was performed by active listening. Our results prove that P3 amplitude is increased by attention – active listening, careful listening to the signal and counting of different tones. It is known that attention attraction strengthens memory function. Attention resources are required also for comprehension of certain sound objects between many others (Zaltz et al., 2002). Our results, just like Polish (2007), Näätanen (2011) reports verify that attention mechanisms in CAEP component P3 generating have significant meaning – they increase amplitude of component P3 but reduces their latency in all patient groups.

For latency of component P3 there is not found correlation with age group that would testify that P3 latency changed proportionally by years. Correlation between component P3 latency and signal and signal/ noise level for elder people in comparison with young people that is reflected in our investigation is not found also in other investigations. Results of *Brown et al.* (1983) cortical auditory evoked potentials testify that latencies of component P3 are longer for people in age of 65 years, but in later survey they have not approved (Brown et al., 2010).

For analysis of complex sound signal there is required greater time of reception in order to activate the involved tissues and it impacts latency of component P3. In Mueller et al. (2008) investigations it is concluded that these processes took place in sensorimotor and somatosensory cortex and beside frontal, parietal and temporary lobule that is related to sound stimuli analysis and reception speed.

When listening actively, the investigatory subject has assignment, for instance, to count different stimuli in order to activate attention to acoustic signal. Maximal P3 response is obtained from electrodes that are located more latterly from the head central line – from parietal scalp electrodes (Freigag et al., 2011). In our investigation – laterally from Cz, i.e. in position C3 and C4. This tendency was mainly observed for elder patients. Changes of signal generation localisation by increase of age may be explained by extension of cortex zone that is involved in central auditory processing due to increase of associative relations. It complies with the speech reception investigation results that testify that incomplete speech reception is compensated by associative comprehension (Yeung & Wong, 2007; Polich, 2007).

Measuring of cortical auditory evoked potentials with help of electrodes reflect sum of head surface activity that is partially made also by clinging layers of cortex (Näätanen & Picton, 1987). Generators of the evoked potentials slightly changes during the life. It is evident by dependence of pike amplitude size on electrode localisation on scalp in different age groups (Bellis, 2003).

Certain differences in amplitude for different age groups are characteristic to the late component P3. P3 amplitude is greater for young people than to elder people and children (Polich, 1996). The results of our investigation are similar: component P3 with greater amplitude exists for control group people with good audition and for young patients, but P3 latencies are extended in group of young patients and elder patients that is associated with auditory disorders.

Amplitudes and latencies of P3 component are associated with sound stimulus properties, attention and brain energy that is required for operative memory (Nieuwenhuis et al., 2005; Martin et al., 2005). P3 latencies, when listening actively to complex signal, are mainly reduced to people with normal audition and less – to younger patients. In its turn attention increase in elder patient group does not impact latency of component P3 or even extends it. In our investigation, when listening without attention to stimuli, amplitudes of component P3 were smaller, in separate cases – even hard to identify. Our results indicate that P3 component reflects less the automatic, but mainly cognitive function that complies with the results of many investigations. Latency of component P3 is mainly extended by noise, but less – by signal intensity (Naatanen et al., 2011, Polich, 2007). The most noticeable impact of noise, extending P3 latency in our investigation was detected in patient groups and particularly in young patient group.

When investigation relation between signal perception and cortex auditory activity we analysed correlation of speech audiometry results with CAEP component P3 latency. P3 is considered to be cognitive, neurophysiological response related to attention, as well as speed parameter of acoustic signal analysis. One of the terms of reference for this work was to survey if P3 latency correlates with speech reception threshold that was approved during the investigation.

The fact that not always a linear relation is stated between increase of stimulus intensity and reduction of evoked potential latency testifies that central neurophysiological function is impacted by yet completely not investigated neurobiological changes.

4.2.3. Limit values of CAEP latencies

When analysing cortical auditory evoked potentials component latencies for control group and patient group, limit values were determined for each CAEP component P1, N1, P2, N2 and P3, specifying latency value that helps to differ the results that complies to normal audition and auditory disorders.

Limit values were determined using method of data statistical analysis – ROC curves.

Using CAEP procedure parameters used in our investigation, the obtained results testify that most sensitive measuring is component P3 latency, the other most sensitive measuring – component N2 latency, both with high specificity. Slightly less sensitive parameter is limit values of component N1, P1 and P2, although specificity for them is high.

We surveyed CAEP latencies for people with normal audition and people with auditory disorder that gave possibility to obtain information about determined limit between normal audition and acoustic signal reception disorders by comparison of data for subjects with different auditory processing.

4.3. Correlations between speech audiometry and CAEP latencies

In our investigation we analysed correlations of electrophysiological and speech audiometry results.

Correlation between latency of component P3 and speech recognition threshold was determined for all the investigation groups. Correlation of component P3 latency with speech recognition threshold in noise was found only to participants of control group with good audition.

Increase of speech recognition threshold in masking noise is not directly related to age (Brown et al., 2010). The greater number of correct replies in dichotic word test correlates with shorter latency of component P3 diagnostically significantly, disclosing compliance of psychoacoustic and electrophysiological measuring.

Our results approve that these two methods are comparable. Latency of component P3 reflects speech reception threshold and could be objective parameter of speech recognition ability.

The results show that in generation of CAEP component P3 the attention mechanisms have significant meaning – they reduce latency of component P3 and enlarge amplitude. Attention resources are required so that certain sound object may be received between many others (Wood & Cowan, 1995).

In our investigation we determined that correlation between latency of component P3 and dichotic digit word recognition in patient groups. It verifies association of CAEP component P3 with speech reception. It proves that both methods approve speech reception disorder and P3 latency as objective investigation may be used for central auditory processing assessment.

Speech audiometry is subjective method and closely related to cognitive function. Speech reception test requires greater participation, there is also language limitation. However, correctly executed speech audiometry provides real result characterising audition function – speech reception threshold.

Although cortical auditory evoked potentials are objective investigation, this method reflects neurophysiological mechanisms of audition. The survey shows, which of speech audiometry tests positively correlate with CAEP component latencies, thus these CAEP components could be used as permanent objective criteria for diagnostics of central auditory disorder.

4.4. Impact of medical therapy on speech audiometry and CAEP results

Until now there are no guidelines and unitary conception for medical therapy of central auditory disorders and there were no investigations about medicine used for treatment of central auditory disorder, but there are executed CAEP investigations for assessment of psychotropic medicine efficiency, associating their efficiency with disease symptoms (Asato et al., 1999). It may be referred also to our investigation of central auditory processing.

Neurochemical impact that succeeds neuron metabolism of brain tissues and neuroprotection as well as neurotransmission would be indicated ethiopathogenetically for improvement of central auditory processing (Colquhoun et al., 1990; Mitra et al., 2001).

We ordinated to our investigation patients nicergoline and pramiracetam – pharmacological remedies that have been approves as having promoting activity for neuroplasticity process in cortex (Pugsley, 1983; Winblad, 2005).

Our investigation patient group participants used remedies – nicergoline of 30 mg per day for 90 days and pramiracetam of 600 mg per day for 40 days. After therapy couse – three months after its beginning – we performed speech audiometry and measuring of cortical auditory evoked potentials and assessed the impact of medically caused neurochemical modulation on psychoacoustics and neurophysiology of acoustic information analysis.

After therapy course the patients marked that subjectively audition sense and speech reception has improved. No by-effects of remedies were observed.

After therapy course, dichotic word and dichotic numeral word reception by both ears statistically credibly improved in both patient groups. Besides, prevalence of right ear significantly reduced (from 20 % up to 8 %) that was similar to parameter of control group.

Pugsley (1983) discovered that racetams together with remedies extending blood vessels efficiently improve cognitive functions.

Our results comply with reports of the positive impact of these remedies in investigations of remedy efficiency for cognitive disorders (Saletu et al.,1995; Battaglia et al., 1989).

In our investigation, the latencies of cortical auditory evoked potentials (CAEP) components reduced in both patient groups after usage of pramiracetam and nicergoline. Latency of CAEP significantly reduced for component P3 in both patient groups, besides greater positive changes showed the results of young group patient. It indicates that young people would have more intensive neurobiological compensation mechanism and neuroplasticity, if the disorder is related to neuron metabolism of cortex.

Results of our survey testify that in the result of neurochemical changes neuron populations generated cortical auditory evoked potentials in shorter time after beginning of stimuli. Analysis of electro-physiologically positively changed acoustic stimuli testifies about favourable dynamic changes in neuron function, aspiring to compensate function deficit.

During investigation it is concluded that both methods are important – psychoacoustic and electrophysiological, because each of them reflects central auditory processing in different aspect. CAEP as objective method supplements and justifies results of speech audiometry.

By combination of psychoacoustic and electrophysiological method there is developed and patented method for diagnostics of central auditory disorders. Methods are clinically approbated and established for practical usage.

CONCLUSIONS

1. Speech audiometry and cortical auditory evoked potentials are investigation methods of informative central auditory processing.

2. The established speech audiometry tests are original sentence tests for determination of speech recognition threshold, dichotic word and dichotic numeral word tests in Latvian. The developed speech audiometry method is successfully usable for assessment of central auditory processing.

3. The established procedure of cortical auditory evoked potentials measuring is diagnostically informative and usable in clinical practice. The determined limit values of cortical auditory evoked potentials component P1, N1, P2, N2 and P3 latencies are considerable as diagnostic criteria for central auditory disorders.

4. Increased speech reception threshold in noise for 5 decibels in comparison with it without noise, dichotic speech reception less than for 90 %, increased prevalence of the right ear for more than 8 % are criteria of central auditory processing disorders.

5. Extended latency of cortical auditory evoked potentials P3 in masking noise in comparison with conditions without noise is sign of central auditory damage.

6. Correlation of dichotic speech reception and speech reception threshold in masking noise with latency of cortical auditory evoked potentials component P3 approves that component P3 is objective diagnostic criteria for diagnostics of central auditory disorder.

7. Medical therapy with nicergoline and pramiracetam improves speech recognition threshold, dichotic speech reception and reduces latencies of cortical auditory evoked potentials that testify about favourable impact of remedies to central auditory processing.

PRACTICAL RECOMMENDATIONS

1. To patients with complains about auditory disorders that are expressed by encumbered speech reception it is recommended to execute speech audiometry and measuring of cortical auditory evoked potentials that is patented method of central auditory disorder investigation.

2. If central auditory disorders are diagnosed – speech recognition threshold is increased, dichotic speech reception is encumbered and latencies of cortical auditory evoked potentials are extended, the medical therapy with nicergoline of 30 mg per day for 90 days and pramiracetam of 600 mg per day for 40 days may be recommended.

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